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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/870,353	05/30/2001	Yan Wang	020130-000111US	8319

20350 7590 04/07/2008
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EXAMINER

HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
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1652

MAIL DATE	DELIVERY MODE
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04/07/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/870,353	Applicant(s) WANG ET AL.	
	Examiner Richard G. Hutson	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 February 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15,17,20,22-30 and 32-44 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15,17,20,22-30 and 32-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants amendment of claims 15 and 30 and the addition of new claims 43 and 44, in the paper of 2/4/2008, is acknowledged. Claims 15, 17, 22-30 and 32 and 34-42 are pending and at issue.

Applicants' arguments filed on 2/4/2008, have been fully considered and are not deemed to be persuasive to overcome the rejections previously applied.

The discussion of the instant application as it relates to the Decision in BPAI Appeal 2008-0763 presented by Applicants representative Mr. Ken Weber, on 4/1/2008, is appreciated.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15, 17, 20, 22-30 and 32-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic-acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein said sequence-non-specific-double-stranded nucleic-acid-binding domain is selected from the group consisting of Sso7d or Sac7d, does not reasonably provide enablement for any protein comprising two heterologous domains

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wherein the first domain is a sequence-non-specific-double-stranded nucleic-acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein said sequence-non-specific-double-stranded nucleic-acid-binding domain comprises an amino acid sequence that has a mere 75% sequence identity to SEQ ID NO: 2 or said sequence-non-specific-double-stranded nucleic-acid-binding domain comprises an amino acid sequence that has a mere 75% identity to the Sac7d sequence set forth in SEQ ID NO: 10. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 15, 17, 20, 22-30 and 32-42. In response to this rejection, applicants have amended claims 15 and 30 and the added new claims 43 and 44, and traverse the rejection as it applies to the newly amended claims. Newly added claims 43 and 44 are included in the rejection for the same reasons previously stated and maintained for claims 15, 17, 20, 22-30 and 32-42.

Applicants continue to traverse this rejection for reasons of record. In brief, Applicants continue to submit that they have provided sufficient guidance in the specification for identifying members of the claimed genus for use in the invention. Applicants submit that the examples in the specification show that both Sac7d and Sso7d work in the claimed invention and that these two proteins, relative to one another, are two of the most divergent members of the naturally occurring family. Applicants continue to submit that, there is extensive information in the art at the time of

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Applicants' invention regarding structure/function analysis of Sac7d and Sso7d that can be used by the skilled artisan to reasonably predict the effects of amino acid changes on function. Applicants submit that the cited art provides further evidence that dsDNA binding activity correlates with the ability to enhance processivity and it is well-settled in the biotechnology art that routine screening of even large numbers of samples is not undue experimentation when a probability of success exists. (*In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). Thus applicants submit that in view of the foregoing and the arguments previously of record in this application, the claims are fully enabled.

Applicants amendment and complete argument is acknowledged, however, not found persuasive for the reasons previously stated and repeated below. It continues that the level of skill in the art is high, although applicants have not provided the guidance necessary to make the genus of proteins claimed, that encompasses those sequence non-specific double-stranded nucleic acid binding domains having a mere 75% sequence identity to the amino acid sequence of SEQ ID NO: 2.

It continues that the amount of guidance provided by applicants specification including applicants cited examples is insufficient to sufficiently enable the claimed genus of proteins comprising any sequence non-specific double-stranded nucleic acid binding domain wherein said sequence non-specific double-stranded nucleic acid binding domain enhances the processivity of an associated polymerase domain. The relationship between the two examples presented by applicants, Sac7d and Sso7d, is acknowledged, however, is insufficient to provide sufficient guidance to enable the

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claimed genus of proteins, having the claimed function. **This insufficiency in guidance is not met by the knowledge in the art.**

As previously stated, the prior art teaches that single point mutations of Sso7d affect the function of the nucleic acid binding domain and renders the art unpredictable. This includes applicant's own post filing art, Wang et al. (Wang et al., Nucleic Acids Research, 2004, vol. 32, p 1197-1207), which teaches the finding that mutational changes in Trp24 of Sso7d significantly reduce its effectiveness in enhancing processivity. Wang et al. further states that the use of a DNA binding protein with a much higher affinity for dsDNA could be detrimental to the catalytic activity of the polymerase and teach that further studies are needed to identify the optimal range of affinities of the dsDNA binding protein to achieve the ultimate balance between processivity and catalysis (page 1205, 1st full paragraph). While it continues to be acknowledged that Wang et al. supports the association between dsDNA binding and the ability to increase the processivity of an associated polymerase, applicant's specification gives no guidance as to how the "level of dsDNA binding" relates to the increase in processivity. As was previously stated, Wang et al. teaches that the use of a DNA binding protein with a much higher affinity for dsDNA could be detrimental to the catalytic activity of the polymerase and teach that further studies are needed to identify the optimal range of affinities of the dsDNA binding protein to achieve the ultimate balance between processivity and catalysis. Thus based upon Wang et al. it is clear that while any associated increase in polymerase processivity is associated with dsDNA

binding activity, applicants have not shown guidance as to how these are related, beyond the fact that they are related.

As previously stated, Shehi et al. (Biochemistry, 2003, vol 42, pp. 8362-8) also supports the unpredictability of the art in that they teach the deletion of Glu53 in Sso7d could not be isolated and suggests that this mutation misfolds the protein and deletion Leu54 in Sso7d has limited solubility in aqueous solution (page 8364, 2nd column, 1st full paragraph). Both mutations demonstrate the unpredictability of the effect of point mutations in Sso7d on any particular function or attribute of Sso7d.

As also stated previously, Consonni et al. (Biochemistry, 1999, vol 38, pp 12709-17) teach the mutation of F31A and W23A in Sso7d impairs the capacity of the protein to bind dsDNA.

Thus while the art teaches an association between dsDNA binding activity and the ability to increase the processivity of an associated polymerase polypeptide, such guidance is not specific beyond the fact that this relationship exists. It continues that a DNA binding protein with a much higher affinity for dsDNA could be detrimental to the catalytic activity of the polymerase and teach that further studies are needed to identify the optimal range of affinities of the dsDNA binding protein to achieve the ultimate balance between processivity and catalysis. Applicants in their analysis have not addressed this relationship between dsDNA binding activity and processivity such that applicants have enabled those proteins having a mere 85% identity to SEQ ID NO: 2.

It continues that the art teaches that sequence similarity alone does not necessarily provide a predictable correlation between the structure and specific function of a protein and applicant's arguments have not addressed the specific function that is the basis of the claims enablement issue. Neither the art nor the specification teach what other domains, regions, or specific amino acids of Sso7d are responsible for sequence non-specific dsDNA binding or more importantly enhancing processivity of an attached polymerase. The prior art supports the unpredictability of this area of technology.

Applicants limited guidance in light of the state and unpredictability of the art leads to the lack of enablement of the claimed genus. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic-acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein said sequence-non-specific-double-stranded nucleic-acid-binding domain comprises an amino acid sequence that has a mere 75% sequence identity to SEQ ID NO: 2 or said sequence-non-specific-double-stranded nucleic-acid-binding domain comprises an amino acid sequence that has a mere 75% identity to the Sac7d sequence set forth in SEQ ID NO: 10. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those proteins having the desired biological characteristics is unpredictable and the

experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rg
4/2/2008

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652